EXHIBIT L

Supplemental Declaration of
Andrew E. Lorincz, M.D.

(filed in co-pending application Serial No. 09/794,456)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: James P. Elia	)	EXAMINER: E.C. Kemmerer, Ph.D.
SERIAL NO.: 09/794,456	)	
FILED: February 27, 2001	)	GROUP ART UNIT: 1646
FOR: METHOD FOR REPAIRING A DAMAGED PORTION OF A HUMAN HEART	)	

SUPPLEMENTAL DECLARATION OF ANDREW E. LORINCZ, M.D.

I, Andrew E. Lorincz, declare as follows:

1. I reside at 13820 NW County Rd 235, Apt 8, Alachua, FL 32616-2098.

2. This Supplemental Declaration is submitted in addition to my previously submitted Declaration in this application, dated June 9, 2003, and makes no changes to such previous Declaration.

3. My Curriculum Vitae is attached as Exhibit A to my previous Declaration.

4. I have read and understood the disclosures of the above-referenced patent application at page 20, line 10 through page 21, line 15; and page 44, line 19 through page 46, line 16. Such disclosures are the same as read and understood by me in my previous Declaration. A copy of such disclosures is attached hereto as Supplemental Exhibit A.

5. I note that the disclosures referenced in above Paragraph 4 relate to using a growth factor for promoting the growth of soft tissue and, more specifically, to a method which may use such growth factors for repairing damaged and dead portions of a human heart by forming new arteries.

6. I have read and understood the claims set forth in Supplemental Exhibit B and have been informed that such claims will be presented to the Patent and Trademark Office in the near future.

7. Based upon above Paragraphs 4-6 and Paragraph 7 of my previous Declaration, it is my opinion that introducing a growth factor to form a new artery in the body of a human patient having a damaged heart will predictably repair a damaged portion of the heart and will also predictably repair a dead portion of such heart.

8. Based upon above Paragraphs 4-6, it is my opinion that one skilled in the medical arts, armed with the knowledge in such paragraphs, would be able to practice the method set forth in Supplemental Exhibit B without need for resorting to undue experimentation. I have been informed that the Examiner has questioned the fact that dosages are not recited in the specification of the above-identified application in connection with the administration of cell growth factors to a human patient with use of intravenous or intraluminal techniques. Such techniques are the subject of claims 16, 17, 30, and 31 in above-mentioned Supplemental Exhibit B. In my opinion, dosages of cellular growth factors to achieve the above-mentioned repair of a human heart are a matter of routine medical practice, requiring only a reasonable degree of experimentation, depending upon such factors as extent of prior heart damage, size of patient, age of patient, health of patient, etc. Consequently, it is my opinion that the disclosure mentioned in Supplemental Exhibit A would enable a person skilled in the medical arts to practice the invention of claims 16, 17, 30, and 31 and predictably anticipate the results defined therein without need for resorting to undue experimentation.

9. Declarant states that the above opinion was reached independently.

Declarant understands that (1) any willful false statements and the like made herein are punishable by fine or imprisonment, or both (18 U.S.C. 1001) and may jeopardize the validity of the application or any patent issuing thereon, and (2) that all statements made of Declarant's own knowledge are true and that all statements made on information and belief are believed to be true.

Further Declarant sayeth not.

Date: 2-3-04

Andrew E. Lorincz

Andrew E. Lorincz

SUPPLEMENTAL EXHIBIT A

DISCLOSURES
APPLICATION SERIAL NO. 09/794,456

PAGE 20, LINE 10 – PAGE 21, LINE 15

Growth factors can be utilized to induce the growth of "hard tissue" or bone and "soft tissues" like ectodermal and mesodermal tissues. As used herein, the term growth factor encompasses compositions and living organisms which promote the growth of hard tissue, such as bone, or soft tissue, in the body of a patient. The compositions include organic and inorganic matter. The compositions can be genetically produced or manipulated. The living organisms can be bacteria, viruses, or any other living organism which promote tissue growth. By way of example and not limitation, growth factors can include platelet-derived growth factor (PDGF), epidermal growth factor (EGF), fibroblast growth factor (acidic/basis (FGF a,b), interleukins (IL's), tumor necrosis factor (TNF), transforming growth factor (TGF-B), colony-stimulating factor (CSF), osteopontin (Eta-1 OPN), platelet-derived growth factor (PDGF), interferon (INF), bone morphogenic protein 1 (BMP-1), and insulin growth factor (IGF). Recombinant and non-recombinant growth factors can be utilized as desired. Bacteria or viruses can, when appropriate, be utilized as growth factors. For example, there is a bacterial hydrophilic polypeptide that self-assembles into a nanometer internal diameter pore to build a selective lipid body. Various enzymes can be utilized for the synthesis of peptides which contain amino acids that control three-dimensional protein structure and growth. Growth factors can be applied in gels or other carriers which regulate the rate of release of the growth factors and help maintain the growth factors and the carrier, at a desired location in the body. Time release capsules, granules, or other carriers containing growth factor can be activated by tissue pH, by enzymes, by ultrasound,

by electricity, by heat, by selected *in vivo* chemicals or by any other selected means to release the growth factor. The carrier can be resorbable or non-resorbable. Or, the growth factor itself can be activated by similar means. Either the carrier or the growth factor can mimic extracellular fluid to control cell growth, migration, and function. The growth factor can be administered orally, systemically, in a carrier, by hypodermic needle, through the respiratory tract, or by any other desired method. The growth factor an also be administered into a capsule or other man-made composition or structure placed in the body. While administration of the growth factor is presently usually localized in the patient's body, circumstances may arise where it is advantageous to distribute a growth factor throughout the patient's body in uniform or non-uniform concentrations. An advantage to growth factors is that they can often, especially when in capsule form or in some other containment system, be inserted to a desired site in the body by simply making a small incision and inserting the growth factor. The making of such small incision comprises minor surgery which an often be accomplished on an out-patient basis. The growth factors can be multifactorial and nonspecific.

PAGE 44, LINE 19 – PAGE 46, LINE 16

Genetic material comprising a portion of a gene, a gene, genes, a gene product (i.e., a composition a gene causes to be produced like, for example, an organ-producing growth factor), growth factor, or an ECM (extracellular matrix) can be used in or on the body to grow an organ to tissue. For example, the vascular epithelial growth factor gene (VEGF) or its growth factor equivalent can be inserted into the body to cause an artery to grow. When insertion of a gene, portion of a gene, gene product, growth factor, or ECM *in vivo* or *ex vivo* is referred to herein in connection with any of the implant techniques of the invention, it is understood that a cell

nutrient culture(s), physiological nutrient culture(s), carrier (s), enhancer(s), promoter(s), or any other desired auxiliary component(s) can be inserted with the gene or at the same location as the gene, growth factor, ECM, etc.

An artery is an organ from the circulatory system. An artery can be grown in the heart, legs, or other areas by injecting a gene or other genetic material into muscle at a desired site. Size, vascularity, simplicity of access, ease of exploitation, and any other desired factors can be utilized in selecting a desired site. The gene is one of several known VEGF genes which cause the production of vascular endothelial growth factors. Several VEGF genes which produce vascular endothelial growth factors are believed to exist because nature intends for there to be several pathways (i.e., genes) which enable the production of necessary growth factors. The existence of several pathways is believed important because if one of the genes is damaged or inoperative, other similar genes can still orchestrate the production of necessary growth factors. VEGF genes are used by the body to promote blood vessel growth. VEGF genes are assimilated (taken in) by muscle cells. The genes cause the muscle cells to make a VEGF protein which promotes the growth of new arteries. VEGF proteins can be made in a lab and injected into a patient intravenously, intraluminally, or intramuscularly to promote the growth of an artery. Or, the genes (or other genetic material) can be applied with an angioplasty balloon, with the assistance of a vector, or by any other method.

It is not always desirable to grow a completely new organ. Sometimes growing a portion of an organ is desirable. For example, in some heart attacks or strokes, a portion of the heart or brain remains viable and a portion dies. An injection of a gene to form cardiac muscle and/or an injection of a gene to form an artery can be utilized to revive or replace the dead portion of the heart. The dead portion of the heart may (or may not) be used as a matrix while the new muscles

and vessels grow. Thus, in this example, a partial new organ is grown in a pre-existing organ. A pacemaker may (or may not) be necessary. A second injection of a gene may (or may not) be necessary to stop cardiac muscle growth once it is completed. Portions of organs throughout the body can similarly be repaired or replaced. It may be necessary to provide gene(s) or growth factor(s) sequentially. For instance, one or more blood vessels are grown by inserting an appropriate gene or other genetic material into a selected area. Second, an appropriate gene or other genetic material is inserted in the selected area to grow a bone or other organ.

The size and shape limitation of the desired structure can come from a containment and boundary contact inhibition phenomenon or by a chemical inhibition.

A variation on the theme of growing a portion of an organ is as follows: a portion of a heart dies. The pericardium is utilized as a scaffold and seeded with cells and/or genes to grow new muscle, and genes (or other genetic material) to grow new arteries. Immediately adjacent the dead cardiac muscle, onto or into the pericardium, the appropriate cells, genes, and/or growth factors (or other genetic material) are placed. Once the new muscle and blood vessels have grown, the function specific tissue can be applied to the damaged portion of the heart and paced, if necessary, to augment cardiac action. If the surgeon desires, the dead muscle can be removed and the new muscle and blood vessels can be surgically rotated into the excised region and secured. This probably can be done endoscopically. In essence, the pericardium is utilized to allow the new muscle wall to grow. The new muscle wall is then transplanted into the damaged heart wall. This procedure utilizes the body as a factor to grow an organ and/or tissue, after which the organ and/or tissue is transplanted to a desired region. On the other hand, the new muscle wall may integrate itself into the old wall and not require transplantation.

SUPPLEMENTAL EXHIBIT B

CLAIMS
APPLICATION SERIAL NO. 09/794,456

7. A method of repairing a dead portion of a pre-existing heart comprising the steps of: placing a growth factor at a selected area of a human patient; and forming a new artery thereby causing said dead portion of said heart to be repaired.

8. The method of claim 7, wherein said growth factor comprises genetic material selected from the group consisting of a portion of a gene, a gene, a gene product, and an extracellular matrix.

9. The method of claim 8, wherein said genetic material comprises a gene.

10. The method of claim 9, wherein said gene comprises VEGF.

11. The method of claim 7, wherein said growth factor comprises a member selected from the group consisting of cells, cellular products, and derivatives of cellular products.

12. The method of claim 11, wherein said growth factor comprises a cell.

13. The method of claim 12, wherein said cell is multifactorial and non-specific.

14. The method of claim 13, wherein said cell comprises a stem cell.

15. The method of claim 7, wherein said growth factor is placed in said patient by injection.

16. The method of claim 15, wherein said injection is intravenous.

17. The method of claim 15, wherein said injection is intraluminal.

18. The method of claim 15, wherein said injection is intramuscular.

19. The method of claim 7, wherein said growth factor is placed in said patient by a carrier.

20. The method of claim 19, wherein said carrier comprises an angioplasty balloon.

21. A method of repairing a damaged portion of a pre-existing heart comprising the steps of: placing a growth factor at a selected area of a human patient; and forming a new artery thereby causing said damaged portion of said heart to be repaired.

22. The method of claim 21, wherein said growth factor comprises genetic material selected from the group consisting of a portion of a gene, a gene, a gene product, and an extracellular matrix.

23. The method of claim 22, wherein said genetic material comprises a gene.

24. The method of claim 23, wherein said gene comprises VEGF.

25. The method of claim 21, wherein said growth factor comprises a member selected from the group consisting of cells, cellular products, and derivatives of cellular products.

26. The method of claim 25, wherein said growth factor comprises a cell.

27. The method of claim 26, wherein said cell is multifactorial and non-specific.

28. The method of claim 27, wherein said cell comprises a stem cell.

29. The method of claim 21, wherein said growth factor is placed in said patient by injection.

30. The method of claim 29, wherein said injection is intravenous.

31. The method of claim 29, wherein said injection is intraluminal.

32. The method of claim 29, wherein said injection is intramuscular.

33. The method of claim 21, wherein said growth factor is placed in said patient by a carrier.

34. The method of claim 33, wherein said carrier comprises an angioplasty balloon.